Claims

1. A method for reducing electrical disturbance of a cell's resting membrane potential comprising administering an effective amount of a composition comprising an effective amount of a local anaesthetic and of one or more of a potassium channel opener, an adenosine receptor agonist, an anti-adrenergic, a calcium antagonist, an opioid, an NO donor and a sodium hydrogen exchange inhibitor.

2. A method for reducing damage to an cell, tissue or organ following ischaemia comprising administering an effective amount of a composition comprising an effective amount of a local anaesthetic and of one or more of a potassium channel opener, an adenosine receptor agonist, an anti-adrenergic, a calcium antagonist, an opioid, an NO donor and a sodium hydrogen exchange inhibitor.

3. A method for preconditioning a cell or tissue during ischaemia or reperfusion comprising administering an effective amount of a composition comprising an effective amount of a local anaesthetic and of one or more of a potassium channel opener, an adenosine receptor agonist, an anti-adrenergic, a calcium antagonist, an opioid, an NO donor and a sodium hydrogen exchange inhibitor.

4. A method for reducing damage to cells, organs and tissues before, during and following a surgical or clinical intervention comprising administering an effective amount of a composition comprising an effective amount of a local anaesthetic and of one or more of a potassium channel opener, an adenosine receptor agonist, an anti-adrenergic, a calcium antagonist, an opioid, an NO donor and a sodium hydrogen exchange inhibitor.

5. A method for reducing either or both inflammation and clotting in a tissue or organ comprising administering an effective amount of a composition comprising an effective amount of a local anaesthetic and of one or more of a potassium channel opener, an adenosine receptor agonist, an anti-adrenergic, a calcium antagonist, an opioid, an NO donor, a protease inhibitor and a sodium hydrogen exchange inhibitor.

6. A method according to any one of claims 1 to 5 wherein the anti-adrenergic is selected from beta-blockers, such as esmolol, atenolol, metoprolol and propranolol and alpha(1)-adrenoceptor-antagonists such as prazosin.

7. A method according to any one of claims 1 to 6 wherein the opioid is selected from enkephalins, endorphins and dynorphins, preferably an enkephalin which targets delta, kappa and/or mu receptors.

8. A method according to any one of claims 1 to 7 wherein the opioid is a delta opioid receptor agonist, preferably a delta-1-opioid agonists and delta-2-opioid agonists, and most preferably [D-Pen 2, 5] enkephalin (DPDPE).

9. A method according to any one of claims 1 to 8 wherein the calcium antagonist is selected from Amlodipine, nifedipine, nicardipine, nimodipine, nisoldipine, lercanidipine, telodipine, angizem, altiazem, bepridil, amlodipine, felodipine, mibefradil, isradipine, cavero, Bay K 8644(L-type)(1,4-dihydro-26-dimethyl-5-nitro-[2(trifluoromethyl)phenyl]-3-pyridine carboxylic acid (methyl ester)), calciseptine (L-type), omega-conotoxin GVIA (N-type), omega-conotoxin MVIIC (Q-type), cyproheptadine HCl, dantrolene sodium, diltiazem HCl (L-type), filodipine, flunarizine HCl (Ca^{2+}/Na^{+}), fluspirilene (L-type), HA-1077 2HCl(1-(5 isoquinolinyl sulphonyl) homo piperazine.HCl), isradipine, loperamide HCl, manoalide, niguldipine HCl (L-type), nitrendipine (L-type), pimozide (L- and T-type), ruthenium red, ryanodine (SR channels), taicatoxin, verapamil HCl (L-type), Azelnidipine (L-type) methoxy-verapamil HCl (L-type), YS-035 HCl (L-type)N[2(3,4-dimethoxyphenyl)ethyl]-3,4-dimethoxy N-nethyl benzene ethaneamine HCl) and calcium antagonists with AV blocking actions, such as verapamil.

10. A method according to any one of claims 1 to 9 wherein NO donor is either nitric-oxide synthase independent (such as nitroprusside, nitro-glycerine, flurbiprofen or its NO-donating derivative, HCT1026 (2-fluoro-a-methyl[1,1'-biphenyl]-4-acetic acid and 4-(nitrooxy)butyl ester) or nitric-oxide synthase dependent (such as regulator calcium calmodulin and L-arginine).

11. A method according to any one of claims 1 to 10 wherein the sodium hydrogen exchange inhibitor is selected from amiloride, cariporide, eniporide, triamterene and EMD 84021, EMD 94309, EMD 96785, HOE 642 and T-162559.

12. A method according to any one of claims 1 to 11 wherein the adenosine receptor agonist is selected from N^6-cyclopentyladenosine (CPA), N-ethylcarboxamido adenosine (NECA), 2-[p-(2-carboxyethyl)phenethyl-amino-5'-N-ethylcarboxamido adenosine (CGS-21680), 2-chloroadenosine, N^6-[2-(3,5-demethoxyphenyl)-2-(2-methoxyphenyl]ethyladenosine, 2-chloro-N^6-cyclopentyladenosine (CCPA), N-(4-aminobenzyl)-9-[5-(methylcarbonyl)-beta-D-robofuranosyl]-adenine (AB-MECA), ([IS-[1a,2b,3b,4a(S*)]]-4-[7-[[2-(3-chloro-2-thienyl)-1-methyl-propyl]amino]-3H-imidazole[4,5-b]pyridyl-3-yl]cyclopentane carboxamide (AMP579), N^6-(R)-phenylisopropyladenosine (R-PLA), aminophenylethyladenosine 9APNEA) and cyclohexyladenosine (CHA), adenosine A1 receptor agonists (such as N-[3-(R)-tetrahydrofuranyl]-6-aminopurine riboside (CVT-510)), CVT-2759 and allosteric enhancers such as PD81723, N6-cyclopentyl-2-(3-phenylaminocarbonyltriazene-1-yl)adenosine (TCPA), and allosteric enhancers of A1 adenosine receptor, such as 2-amino-3-naphthoylthiophenes.

13. A method according to any one of claims 5 to 12 wherein the protease inhibitor is selected from indinavir, nelfinavir, ritonavir, lopinavir, amprenavir and aprotinin.

14. A method according to any one of claims 1 to 13 wherein the potassium channel opener is selected from nicorandil, diazoxide, minoxidil, pinacidil, aprikalim, cromokulim and derivative U-89232, P-1075, emakalim, YM-934, (+)-7,8-dihydro-6, 6-dimethyl-7-hydroxy-8-(2-oxo-1-piperidinyl)-6H-pyrano[2,3-f] benz-2,1, 3-oxadiazole (NIP-121), RO316930, RWJ29009, SDZPCO400, rimakalim, symakalim, YM099, 2-(7,8-dihydro-6,6-dimethyl-6H-[1,4]oxazino[2,3- f][2,1,3]benzoxadiazol-8-yl) pyridine N-oxide, 9-(3-cyanophenyl)-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione

(ZM244085), [(9R)-9-(4-fluoro-3-125iodophenyl)-2,3,5,9-tetrahydro-4H-pyrano[3,4-b]thieno[2,3-e]pyridin-8(7H)-one-1,1-dioxide] ([125I]A-312110), (-)-N-(2-ethoxyphenyl)-N'-(1,2,3-trimethylpropyl)-2-nitroethene-1,1-diamine (Bay X 9228), N-(4-benzoyl phenyl)-3,3,3-trifluro-2-hydroxy-2-methylpropionamine (ZD6169), ZD6169 (KATP opener) and ZD0947 (KATP opener), WAY-133537, dihydropyridine A-278637 and BK-activators (also called BK-openers or BK(Ca)-type potassium channel openers or large-conductance calcium-activated potassium channel openers) such as benzimidazolone derivatives NS004 (5-trifluoromethyl-1-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-2H-benzimidazole-2-one), NS1619 (1,3-dihydro-1-[2-hydroxy-5-(trifluoromethyl)phenyl]-5-(trifluoromethyl)-2H-benzimidazol-2-one), NS1608 (N-(3-(trifluoromethyl)phenyl)-N'-(2-hydroxy-5-chlorophenyl)urea), BMS-204352 and retigabine.

15. A method according to any one of claims 1 to 14 wherein local anaesthetic is selected from mexiletine, diphenylhydantoin prilocaine, procaine, mepivacaine, Class 1B antiarrhythmic agents, such as lignocaine or derivatives thereof (eg QX-314), and sodium channel blockers such as tetrodotoxin, primaquine, QX, HNS-32 (CAS Registry # 186086-10-2), NS-7, kappa-opioid receptor agonist U50 488, crobenetine, pilsicainide, phenytoin, tocainide, NW-1029 (a benzylamino propanamide derivative), RS100642, riluzole, carbamazepine, flecainide, propafenone, amiodarone, sotalol, imipramine and moricizine, and any derivatives thereof.

16. A method according to any one of claims 1 to 15 wherein the cell is a myocyte, endothelial cell, smooth-muscle cell, neutrophil, platelet and other inflammatory cells, or the tissue is heart tissue or vasculature, or the organ is a heart.

17. A method according to any one of claims 4, or 6 to 15 when dependent from claim 4, wherein the composition further comprises an agent selected from normal or low-molecular-weight heparin (such as enoxaparin), non-steroidal anti-inflammatory agents (such as indomethacin, ibuprofen, rofecoxib, naproxen, celecoxib or fluoxetine), an anti-platelet drug (such as

Clopidogrel), platelet glycoprotein (GP) IIb/IIIa receptor inhibitors (such as abciximab), statins (such as pravastatin), angiotensin converting enzyme (ACE) inhibitors (such as captopril) and angiotensin blockers (such as valsartin).

18. A method according to any one of claims 1 to 17 wherein the composition further comprises one or more of an antioxidant, ionic magnesium, an impermeant and a metabolic substrate.

19. A method according to any one of claims 1 to 18 wherein the composition has been oxygenated.

20. A method according to any one of claims 1 to 19 comprising administering the composition as part of a medicament including the composition and a blood-based or crystalloid carrier.

21. A method according to claim 20 wherein the medicament has concentrations of one or more of sodium, calcium and chloride lower than physiological concentrations.

22. A method according to claim 20 wherein the medicament has concentrations of one or more of sodium, calcium and chloride that have been adjusted from blood physiological concentrations.

23. A method according to any one of claims 1 to 22 wherein the medicament is at a temperature of profound hypothermia (0 to 4 degrees Celsius), moderate hypothermia (5 to 20 degrees Celsius), mild hypothermia (20 to 32 degrees Celsius) or normothermia (32 to 38 degrees Celsius).

24. A method according to any one of claims 1 to 23 wherein the components of the medicament or composition are combined before administration or when the components are administered substantially simultaneously or co-administered.

25. Use of a composition or medicament according to any one of claims 1 to 24.